REMARKS

Claims 1-31 and 38-95 are currently pending in this application. No new matter is being presented by this amendment.

A. Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-31 and 38-95 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with written description. The Examiner asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner refers to the pH ranges of between 2.0 and 3.1, between 2.5 and 3.1, between 2.7 and 3.1 and between 2.7 and 3.1 recited in the pending claims and asserts that the specification lacks written description for the disclosure of these ranges. The Examiner, however, does acknowledge that applicants have disclosed an upper limit of 3.1. Applicants traverse.

The specification defines the relevant pH ranges of the formulation on page 5, lines 28-30, which recites:

> The pH of the formulation according to the invention is between 2.0 and 4.5, preferably between 2.5 and 3.5 and more preferably between 2.7 and 3.3 and particularly preferably between 2.7 and 3.2. Most preferred *are pHs with an upper limit* of 3.1 [emphasis added].

If one of skill in the art were to read this paragraph in view of the application as a whole, the skilled artisan could only conclude that each of the disclosed pH ranges would have a preferred *upper limit* of 3.1. Here, applicants expressly state that most preferred "are pHs with an upper limit of 3.1." Because the verb and noun are plural, "an upper limit" must refer to a recited range. In further support of satisfying the written description criteria, applicants refer to *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976) (*see also* MPEP § 2163.05(III)). In that case, the ranges described in the original specification included a range of "25%-60%" and specific examples of "36% and "50%." A new claim limitation of "at least 35%" was introduced but found not to meet the written description requirement because the phrase "at least" had no upper limit and caused the claim to read literally on embodiments outside the "25% to 60%" range. However, the court ruled that a limitation to "between 35% and 60%" did meet the written description requirement (also see

MPEP 2163.05(III)). In the current application, applicants expressly recite an upper pH limit of 3.1 and therefore, written description is clearly met. For this reason, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

B. Rejections under 35 U.S.C. § 102(b):

(1) Claims 1-31, 50, 53-80 and 93 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Freund *et al* (DE 19653969, hereinafter "Freund") (US 2001/0008632 being used as the translation for the German document). Applicants traverse.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co.*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); *see also* MPEP § 2131. Moreover, prior art which teaches a value or range that is very close to, but does not overlap or touch the claimed range does not anticipate the claimed range (*Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985); *see also* MPEP. § 2131.03(III)).

Here, Freund does not disclose the presently claimed limitation of "acid for achieving a pH between 2.0 and 3.1." Although Freud discloses solutions that are set to a pH of 3.2 to 3.4 with 0.1 N HCl (see ¶¶ 48, 50 and 55), this pH range does not overlap or touch the claimed range. Thus, claims 1-31, 50, 53-80 and 93 are patentable. Applicants respectfully request withdrawal of this rejection.

(2) Claims 1-31, 50, 53-80 and 93 stand rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Bozung *et al.* (DE 19921693; hereinafter "Bozung")(U.S. 6,433,027 being used as a translation thereof). Applicants traverse.

Bozung does not disclose the presently claimed limitation of "acid for achieving a pH between 2.0 and 3.1." Although Bozung discloses a formulation with a pH of 3.4 (see col. 7, lines 20-31), this pH does not overlap or touch the claimed range. Thus, claims 1-31, 50, 53-80 and 93 are patentable. Applicants respectfully request withdrawal of this rejection.

C. Rejections under 35 USC 103(a)

Claims 38-49, 51-52, 81-92 and 94-95 stand rejected under 35 U.S.C. § 103(a), as being unpatentable over Freund as applied to claims 1-31, 50, 53-80 and 93 above, and further in view of Weston *et al.* (WO 91/14468, hereinafter "Weston"). Applicants traverse.

Three Criteria Needed For A *Prima Facie* Case of Obviousness Are Not Met (MPEP § 2142)

A proper obviousness analysis involves a three-step process. First, the Examiner must establish a *prima facie* case of unpatentability based on obviousness. If a *prima facie* case is established, the burden shifts to the applicant to come forward with rebuttal evidence or argument to overcome the *prima facie* case. Finally, the Examiner should evaluate the totality of the facts and all the evidence to determine whether the claimed invention would have been obvious. MPEP § 2144.08 (II).

The standard for obviousness is set out in *Graham v. John Deere Co.* and is based on several underlying factual inquiries, including (1) determining the scope and content of the prior art, (2) resolving the level of skill of a person of ordinary skill in the art, (3) ascertaining the differences between the claimed invention and the teachings of the prior art, and (4) evaluating any objective indicia of non-obviousness, e.g., long-felt need, commercial success, failure of others, copying, unexpected results or other secondary considerations (383 U.S. 17-18, 86 S.Ct. 684).

In considering and determining patentability under 35 U.S.C. § 103, Patent Examiners are responsible for applying the *Graham* factors in each and in every case (MPEP § 2141(I)). Moreover, the Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness, which is established by meeting three basic criteria – (1) suggestion or motivation to modify the reference or to combine reference teachings, (2) reasonable expectation of success and (3) prior art reference (or references when combined) must teach or suggest all the claim limitations (MPEP § 2142). As discussed below, the Examiner's combinations of a primary reference with a secondary reference does not meet the requirements necessary to establish a *prima facie* case of obviousness.

Applicants' claim 1 recites a pharmaceutical preparation comprising tiotropium or pharmaceutical salt thereof in a concentration of between 0.0005 and 5% by weight, a solvent selected from water or a water/ethanol mixture; acid for achieving a pH between 2.0 and 3.1 and a pharmaceutically acceptable preservative, wherein the preparation optionally includes a pharmacologically acceptable complexing agent, a stabilizer, a pharmacologically acceptable cosolvent, or other pharmacologically acceptable adjuvants and additives. Claims 2-31 depend directly or indirectly from claim 1. Claim 50 relates to a method of treating asthma or COPD comprising administering the pharmaceutical preparation according to claim 1. Claim 53 is similar to claim 1 and claims 54-80 depend directly or indirectly from claim 53. Claim

93 relates to a method of treating asthma or COPD comprising administering the pharmaceutical preparation according to claim 53.

Applicants claim 38 is directed to a method for administering a pharmaceutical preparation according to claim 1, comprising nebulilzing the preparation in an inhaler selected from the group consisting of an inhaler according to the Weston Nebulizer or an inhaler according to the Jaeger Nebulizer B. Claim 39 relates to a method for administering a pharmaceutical preparation according to claim 1, comprising nebulilzing the preparation in an inhaler which nebulizes defined amounts of the preparation (pressures and nozzle dimensions described). Claims 40-49 depend directly or indirectly from either claim 38 or 39. Claims 51 and 52 relate to a method of treating asthma or COPD comprising administering the pharmaceutical preparations using the methods of claims 38 and 39 respectively. Claims 81 and 82 are similar to claims 38 and 39 except that they refer to the pharmaceutical preparation of claim 53. Claims 83-92 depend directly or indirectly from either claim 81 or 82. Claims 94 and 95 relate to a method of treating asthma or COPD comprising administering the pharmaceutical preparations using the methods of claims 81 and 82 respectively.

The Examiner has maintained rejection of claims 38-49, 51-52, 81-92 and 94-95 for obviousness because, although Freund lacks specific teachings of the presently claimed inhalation device, Weston allegedly cures this defect. As discussed above, Freund does not teach or suggest the invention as recited in pending claims 1-31, 50, 53-80 and 93, specifically with regard to the stability of tiotropium in the pH range of 2.0-3.1. In fact, Freund teaches that the pH of its formulation is in the range of 3.2-3.4. Freund does not state that the pH value is of no relevance but instead, Freund discloses the pH range of 3.2-3.4 to be important for its formulation (see ¶¶ 48, 50 and 55), wherein tiotropium is just one of a number of active substances mentioned in Freund. Freund is silent with respect to the dependence of tiotropium stability on pH and provides no motivation to leave the disclosed pH range of 3.2-3.4. In contrast, the presently claimed invention teaches that the pharmaceutical preparation of tiotropium has a preferred upper pH limit of 3.1.

Moreover, Weston and Freund differ significantly in their teachings. For example, Weston is directed to propellant-driven devices and methods, whereas Freund discloses propellant-free solutions. One of skill in the art would appreciate that these are different technological fields and would not simply combine their disclosures because of this

difference. As a result, there is neither a motivation to combine nor an expectation of success. Additionally, the prior art references when combined do not teach or suggest all the claim limitations. This is especially true because Freund's pH range falls outside the range taught by the present claims and does not suggest that there may be additional benefits of lowering pH. For these reasons, the three criteria for a *prima facie* conclusion of obviousness are not met and applicants respectfully request withdrawal of this rejection.

D. Obviousness-type Double Patenting

(1) Claims 1-31 and 38-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-81 of US 6,890,517 B2 (hereinafter "the '517 patent"). While not agreeing with the propriety of the Examiner's rejection and solely to advance prosecution, a terminal disclaimer has been filed over the claims of the '517 patent, thus removing the double patenting rejection.

(2) Claims 1-31, 50, 53-80 and 93 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of US 6,908,928 in view of Freund. As discussed above, Freund does not recite a pharmaceutical preparation comprising tiotropium with a pH range of between 2.0 and 3.1. As such, applicants kindly request that the Examiner reconsider this rejection in light of the arguments made above.

E. Conclusion

Applicants submit that the pending claims are allowable and respectfully solicit that a Notice of Allowance be issued for these claims. If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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